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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT PAPER NUMBER

1624

DATE MAILED: 08/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/647,156

Applicant(s)

STENKAMP ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) 4,5,7,8,12,14,15,17-19,24,25,31 and 33-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6,9-11,13,16,20-23,26-28,32 and 44 is/are rejected.
- 7) ☒ Claim(s) 29 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6/18/04 + 2/10/06.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

NON-FINAL ACTION

It is acknowledged that applicants have elected with traverse Group I (claims 1-3, 6, 9-11, 13, 16, 20-23, 26-30, 32 and 44 (in part)) in the reply of 4-7-06. The traversal is on the ground that Groups 1 and 2 should be combined due to structural similarity. Said traversal is not found persuasive because the position of the ring atom "U" is different for formulae 1-1 and 1-2. Thus, the substituents on the ring containing "U" are also at different positions for formulae 1-1 and 1-2. Consequently, the structural search for formula 1-1 would not yield an answer set for formula 1-2. References that could anticipate or render obvious formula 1-1 would not do so to formula 1-2. Therefore, the restriction is deemed proper, and made FINAL.

The examiner will not search and considered other groups.

Claims 1-44 are pending.

Claims 4, 5, 7, 8, 12, 14, 15, 17-19, 24, 25, 31 and 33-43 are withdrawn from consideration as being drawn to the non-elected subject matter.

Claims 1-3, 6, 9-11, 13, 16, 20-23, 26-30, 32 and 44 (in part) are considered herein.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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1. **Scope of Enablement:** Claims 1-8, 11-13, 15, 16, 20-22, 26-28, 32 and 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of compounds of formula I (or 1-1) wherein:

- i. A and Y are phenyl or pyridyl **not** extensively substituted;
- ii. W is a bond;
- iii. Z is an alkylene chain;
- iv. B is phenyl;
- v. R^1 - R^3 are **not** extensively substituted, or **not** forming a bridge or a ring with another variable.

does not reasonably provide enablement for compounds of formula I (or 1-1) wherein:

- vi. A and Y are phenyl or pyridyl that extensively substituted;
- vii. W and Z are other groups or extensively substituted;
- viii. B is another ring;
- ix. R^1 - R^3 are extensively substituted

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The Breadth of the claims: Claims 1 recites carboxamide compounds of formula I having a total of 9 variables including R^1 , R^2 , X, Y, Z, R^3 , A, W and B. Each variable represents a set of substituents that are further substituted with other variables such as R^4 - R^9 , R^{11} - R^{14} which in turn are defined by other variables such as R^{15} - R^{22} . Besides the extensive list of substituents, R^1 and R^2 can form a alkylene bridge which can be further substituted. Likewise, X and R^1 can form a ring that can also be substituted. Similarly, Z and R^3 can form a ring, or A and R^3 can also form a ring which consisting of another set of variables including Q and L^1 - L^3 . Furthermore, variables R^1 - R^9 , R^{11} - R^{22} , X, Y, Z, A, W and B can have additional substituents. Thus, formula I represents a myriad of permutations of incredibly complicated structures in terms of functional groups, bridge, rings, or combination thereof, and substituents on top of substituents. It is clear, then, the scope of formula I is unduly broad.

Claims 2-8, 11-13, 15, 16, 20-22, 26-28, 32 and 44 depend on claim 1, and still have fairly broad scope of formula I.

The amount of direction or guidance presented: Although the specification provides a generic scheme that appears to teach all conceivable compounds of formula I, such a scheme does not adequately accommodate the addition of various substituents which require sources of starting materials or additional steps with appropriate reagents and reaction conditions. Working examples also describe the process of making compounds of formula 1-1 wherein A and Y are mostly **phenyl** rings with no additional substituents, and linking groups such as Z and W are not extensively substituted. That is, the specification is silent as to the availability of necessary reactants needed to prepare a compound of formula I with a complicated structure comprising various functional groups, bridge, rings or combination thereof, and can be substituted as well as further substituted. Note, **In re Howarth** 210 USPQ 689; **Ex parte Moersch** 104 USPQ 122, for the need to show starting material sources commensurate with the claims' scope.

Thus, the specification does not provide sufficient enablement commensurate with the broad Markush group of the claimed formula.

The state of the prior art: There is no reference teaching a compound analogous to a compound of formula I (or 1-1). No starting material for various variables and their substituents has been taught, and no reaction condition has been revealed. Furthermore, it is not known if such a compound would possess any biological activity. Thus, the state of the prior art does not support the preparation and/or use for the broad scope of the claimed formula I (or 1-1).

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select the proper starting material for making compounds of formula I (1-1) with so many variables and substituents. In addition, one would have to determine biological activity in terms of an IC_{50} value, LD_{50} , therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I (or 1-1), such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case the with no starting material disclosed as well as no reaction conditions taught for adding various substitutents to the core, the skilled chemist would have to carry out undue experimentation to make compounds of the claimed formula.

Note, the Federal Circuit has repeatedly held that “the specification must teach those skilled in the art how to make and use the **full scope** of the invention without ‘undue experimentation’”.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-3, 6, 9-11, 13, 16, 20-23, 26-28, 32 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. It is not clear what ring or ring system is formed by R^1 and R^2 . Since X can also form a ring with R^1 , would the combination of R^1R^2 -N- and X form a fused ring.

Likewise, Z is a linking group (e.g., $-\text{CH}_2\text{CH}_2-$), it is unclear what type of ring it can form with R^3 . Likewise, R^3 can also form a ring with Y which is a ring itself, so it is unclear if a fused ring is intended. Thus, all these possible rings with no definite structure render formula I indefinite metes and bounds.

b. Formula I has variables that are defined by other variables which have substituents that can be further substituted. Thus, it is unclear what possible final structure of the claimed compound is.

c. The last paragraph of claim 1, it is unclear if the listed substituents are additional substituents on the variables themselves, or are they substituents on the substituents of those variables.

d. The limitation of "group which can be cleaved in-vivo" has indefinite metes and bounds because it is unclear what constitutes such a group. The specification does not define such a group, nor does it list what possible functional group can be cleaved in-vivo.

- e. It is not clear if R^6 and R^7 have the same definition as R^8 and R^9 . Likewise, it is not clear if R^{25} has the same definition as R^{26} and R^{27} .
- f. Claim 13 lacks antecedent basis because it depends on claim 1, but recites groups such as: “2-hydroxyethyl”, “3-hydroxy-n-propyl”, “2-hydroxy-methyl-ethyl”, which are not recited in claim 1.
- g. The scope of R^{23} and R^{24} of formula 1-1 does not seem to be within the scope of X in claim 1.
- h. Claim 44 recites the word “preferably” which renders the claim indefinite because it is not clear if recitation followed said term is a limitation.
- i. Claims 2-3, 6, 9-11, 13, 16, 20-23, 26-28, 32 and 44 are rejected as being dependent on claim 1 and still recite the indefinite limitations,.

Claim Objections

- 3. Claims 29 and 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 29 and 30 recite species of formula (1-1) having a biphenyl group and a combination of substituents that are not taught or fairly suggested by the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

8-3-06



Tamthom N. Truong
Examiner
Art Unit 1624



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